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Hartmann, Matthias N ; Kluge, Agne ; Kalis, Annemarie ; Mojzisch, Andreas ; Tobler, Philippe N ;  
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## **Apathy in Schizophrenia as a Deficit in the Generation of Options for Action**

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## Abstract

Negative symptoms are a core feature of schizophrenia and have been grouped into two factors: a motivational factor, which we refer to as *apathy*, and a *diminished expression* factor. Recent studies have shown that apathy is closely linked to functional outcome. However, knowledge about its mechanisms and its relation to decision-making is limited. In the current study, we examined whether apathy in schizophrenia is associated with predecisional deficits, that is, deficits in the generation of options for action. We applied verbal protocol analysis to investigate the quantity of options generated in ill-structured real world scenarios in 30 patients with schizophrenia or schizoaffective disorder and 21 healthy control participants. Patients generated significantly fewer options than control participants and clinical apathy ratings correlated negatively with the quantity of generated options. We show that the association between measures of psychopathology and option generation is most pronounced in regard to apathy symptoms and that it is only partially mediated by deficits in verbal fluency. This study provides empirical support for dysfunctional option generation as a possible mechanism for apathy in schizophrenia. Our data emphasize the potential importance of predecisional stages in the development and persistence of apathy symptoms in neuropsychiatric disorders and might also inform the development of novel treatment options in the realm of cognitive remediation.

*Keywords:* schizophrenia, negative symptoms, option generation, decision-making, cognitive effort

### Apathy in Schizophrenia as a Deficit in the Generation of Options for Action

Negative symptoms are a core feature of schizophrenia (Kraepelin, 1919) and include avolition, anhedonia, asociality, blunted affect, and alogia (Blanchard & Cohen, 2006; Strauss et al., 2012). They are strongly linked to poor functional outcome and patient's quality of life (Faerden et al., 2009; Fervaha, Foussias, Agid, & Remington, 2013; Kiang, Christensen, Remington, & Kapur, 2003). However, knowledge about causal mechanisms and treatment options remain limited (Erhart, Marder, & Carpenter, 2006; Stahl & Buckley, 2007).

There is now a consensus that negative symptoms can be grouped into two factors (Blanchard & Cohen, 2006; Foussias & Remington, 2010; Messinger et al., 2011). First, a motivational factor, which we refer to as *apathy*, combining avolition, anhedonia, and asociality. Second, a *diminished expression* factor that consists of the symptoms of blunted affect and alogia. Accumulating evidence suggests that among the two negative symptom factors, apathy is more strongly linked to functional outcome (Fervaha, Foussias, et al., 2013; Strauss et al., 2013), thus emphasizing the need for a better understanding of apathy in schizophrenia to improve treatment.

Empirically, apathy can be defined as a quantitative reduction in goal-directed behavior (Brown & Pluck, 2000; Levy & Dubois, 2006). Recent schizophrenia research has attempted to explain the patients' reduction in goal-directed behavior with dysfunctional decision-making (Fervaha, Graff-Guerrero, et al., 2013; Hartmann et al., in press; Heerey, Bell-Warren, & Gold, 2008). These approaches, including our own, have mainly conceptualized decision-making as the evaluation and selection of options for action. Critically, these approaches presuppose that options for decision-making are already at hand, which however is rarely the case in everyday situations. Normally, options for action in a given situation have to be generated first. It is thus

conceivable that deficits in the ability to generate options for action might lead to apathy as a quantitative reduction in goal-directed behavior.

To illustrate, imagine the situation where you have missed your train and you have one hour waiting time. This scenario is an example of a real world decision-making situation, which lacks essential structural elements, such as a clear goal or available operators to reach the goal (Gettys, Pliske, Manning, & Casey, 1987). Such decision situations have been referred to as *ill-defined* or *ill-structured* in the early problem solving literature (e.g., Reitman, 1964). In order to make a choice, viable options have to be generated, and then evaluated in terms of expected utility (i.e.,  $\text{expected value} \times \text{expected probability}$ ). This first step of option generation occurs prior to choice (i.e., *predecisional*) and is particularly important in ill-structured situations. However, decision-making researchers have mostly neglected this fact and have focused on entirely structured decision experiments (e.g., binary choice between gambles). Consequently, it has been proposed that decision-making models should be complemented by a predecisional stage, in which these options for actions are generated (Fellows, 2004; Kalis, Kaiser, & Mojzisch, 2013; Kalis, Mojzisch, Schweizer, & Kaiser, 2008; Smaldino & Richerson, 2012).

Previous research on option generation has mainly employed two different approaches. A first line of research has been motivated by the general problem-solving literature and has investigated option generation in the context of complex decision situations such as a town's parking problem (Adelman, Gualtieri, & Stanford, 1995; Gettys et al., 1987). A second line of research has been motivated by expert decision-making, such as in chess or sport situations (Klein, Wolf, Militello, & Zsombok, 1995; Raab & Johnson, 2007). However, only very few studies have used ill-structured everyday scenarios to study option generation (e.g., Hausser, Schlemmer, Kaiser, Kalis, & Mojzisch, 2014; Kaiser et al., 2013). To our knowledge, no study

has used this approach to investigate potential links between psychopathology and option generation.

Several authors have reasoned that the reduction of goal-directed behavior in apathetic patients could be associated with dysfunctional option generation as a predecisional deficit (Fellows, 2004; Kalis et al., 2008; Sinha, Manohar, & Husain, 2013; Smaldino & Richerson, 2012). The generation of fewer options limits the option space, which in turn might negatively impact the selection of options for goal-directed behavior. However, to our knowledge this hypothesis has not yet been empirically tested with regard to apathy in schizophrenia or other neuropsychiatric disorders. There is evidence that lesions of the prefrontal cortex lead to impaired real-world planning and problem-solving (Channon, 2004; Goel et al., 2013). Interestingly, there is a considerable overlap between these regions and those most consistently associated with apathy after brain lesions. In patients with schizophrenia, only few studies have used ill-structured tasks, which did not explicitly assess option generation (e.g., Evans, Chua, McKenna, & Wilson, 1997; Revheim et al., 2006). To our knowledge no study has looked at the relationship between negative symptoms and option generation in ill-structured decision situations.

In the current study, we hypothesized that patients would generate fewer options compared to control participants and that the severity of apathy symptoms in patients would negatively correlate with the quantity of generated options for action. To test this main hypothesis, we applied an adapted version of a recently described option generation task (Kaiser et al., 2013) using verbal protocol analysis in the context of 20 ill-structured real-world scenarios. To assess option generation in a broad approach and to test secondary hypotheses, we applied a  $2 \times 2$  factorial design. (1) We manipulated the stopping-rule in the option generation

phase, that is, participants either decided on their own when enough options were generated to initiate satisfactory goal-directed action or they were encouraged to generate a maximum number of options. Here we aimed to test whether it is specifically the premature stopping in the process of option generation due to motivational deficits or a general reduction in option generation capacity that is linked to apathy (Barch, 2005). (2) We further designed half of the scenarios as situations with an implicit goal state (problem-solving scenarios), and the other half as scenarios without such (open scenarios). Based on clinical observations that apathetic patients are most strongly impaired in unstructured situations (Treméau, Nolan, Malaspina, & Javitt, 2012), we hypothesize that the association of apathy with quantity of generated options would be more pronounced in the open scenarios relative to problem-solving scenarios.

## Methods

### Participants

Thirty patients meeting DSM-IV (APA, 2000) criteria for schizophrenia ( $n = 24$ ) or schizoaffective disorder ( $n = 6$ , no mood episode) and 21 healthy control (HC) participants took part in the present study. The local Ethics committee approved the study and all participants gave written informed consent. Patients were clinically and pharmacologically stable inpatients at the end of their hospitalization ( $n = 25$ ) or outpatients ( $n = 5$ ) treated at the Psychiatric Hospital of the University of Zurich. Please note that the average inpatient stay for patients with schizophrenia in Swiss psychiatric hospitals is above 40 days (BFS, 2012), therefore many of our inpatients would be treated as outpatients in other health care systems. Importantly, inpatients participated in a multimodal treatment program and were encouraged to engage in activities outside the hospital. Thus, they had the opportunity for a broad range of activities allowing appropriate assessment of negative symptoms. Patients were excluded if (1) daily *lorazepam*

dosage exceeded 1 mg, (2) if florid positive symptoms were present (Positive and Negative Syndrome Scale; PANSS (Kay, Fiszbein, & Opler, 1987); any positive subscale item score > 4), (3) if extrapyramidal symptoms were present on clinical examination or (4) if additional DSM-IV axis I or axis II diagnostic criteria were met (according to the treating clinician). These restrictive criteria were employed in order to reduce possible confounding factors, in particular potential causes for secondary negative symptoms (positive symptoms, extrapyramidal side-effects and depression). To confirm axis I diagnosis in patients, exclude comorbid axis I disorders and ensure the absence of axis I disorders in the HC group, we used the Mini-International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 1998).

### **Clinical Rating Scales**

For the psychopathological characterization of the patient sample the following instruments were used: Brief Negative Symptom Scale (BNSS; Kirkpatrick et al., 2011), PANSS, Personal and Social Performance Scale (PSP; Schaub & Juckel, 2011), Calgary Depression Scale for Schizophrenia (CDSS; Addington, Addington, & Schissel, 1990), and the informant version of the Apathy Evaluation Scale, which was completed by a member of the nursing team (AES; Marin, Biedrzycki, & Firinciogullari, 1991). The BNSS was translated to German by the senior author. An attending psychiatrist who was BNSS-naïve and native English speaking performed the back-translation, which was approved by the authors of the original scale. Both raters in the current study were involved in the validation study of the German Version of the BNSS, which showed excellent interrater-reliability (publication in preparation; intraclass correlation coefficient for the BNSS total score was 0.97; anhedonia: 0.97, distress: 0.93, asociality: 0.95, avolition: 0.88, blunted affect: 0.95, alogia: 0.97). The scores for the two critical negative symptom factors in the BNSS – apathy and diminished expression - were calculated according to



the two-factor structure proposed by the authors of the scale (apathy: average of anhedonia, asociality, avolition; diminished expression: average of blunted affect, alogia; Kirkpatrick et al., 2011; Strauss et al., 2012). Please note that the authors of the scale refer to the two factors as “motivation and pleasure” and “emotional expressivity”. In the present study we use the established terms for the symptom dimensions of “apathy” and “diminished expression” in accordance with other authors (Faerden et al., 2009; Hartmann et al., in press; Kirkpatrick, 2014).

### **Cognitive Assessment**

We assessed cognitive ability for inclusion as a possible confound in our study. Based on our previous research on the cognitive basis of option generation (Kaiser et al., 2013), we included a measure of verbal memory retrieval (VLMT; German version of the Auditory Verbal Learning Memory Test; Helmstaedter, Lendt, & Lux, 2001) and semantic and phonemic fluency (animal naming, s-words; Delis, Kaplan, & Kramer, 2001). We also assessed processing speed (Digit-Symbol Coding; Von Aster, Neubauer, & Horn, 2006), premorbid crystallized verbal intelligence (MWT-B; Lehrl, 1999), and ideation fluency (number of responses on the brick item of the Alternate Uses Test; Guilford, 1967). Each test score was z-transformed based on HC group data.

### **Option Generation Task**

In the option generation task, participants were verbally presented with 20 ill-structured short real-world scenarios for which they had to verbally generate options for action (task adapted from Kaiser et al., 2013; see supplementary material for detailed task instructions and list of scenarios). Participants were specifically instructed to generate goal-directed options. Our

experiment was designed as a 2 (subjective stopping rule vs. maximum)  $\times$  2 (problem solving vs. open scenarios) within-subjects factorial design with five scenarios for each cell.

In the first half of the experiment (10 scenarios), participants were instructed to generate options until they felt confident that they could satisfactorily decide on an option for action (subjective stopping rule). In the second half of the presented scenarios (10 scenarios), participants were instructed to generate as many subjective options as they could think of (maximum). When participants stopped generating options, they were prompted twice to think of additional options (“can you think of other options?”). However, if generation time per scenario exceeded two minutes the experimenter stopped the participant and proceeded with the next scenario. Generation time per scenario was assessed as the time period beginning at the end of scenario presentation until the last option was generated by the participant using a stop watch. The frequency of options per second was then calculated on scenario level as amount of generated goal-directed options divided by generation time.

As a second factor, scenarios were either designed as ill-structured problem-solving scenarios with an implicit desired outcome (e.g., “You are alone in an elevator. Suddenly the elevator gets stuck. What could you do?”), or ill-structured “open” scenarios that do not imply any course of action or goal state (e.g., “The sun shines unexpectedly on your free day. What could you do?”). The second factor was pseudo-randomly manipulated within the two blocks of 10 scenarios each.

### **Data Processing**

Generated options were recorded and later transcribed to spreadsheet software for further analyses. For the statistical analyses the options were divided into options that clearly entailed goal-directed behavior (e.g., “Go to the movies with friends.”) and options that were not goal-

directed (e.g., “Wait and see what happens.”), redundant with respect to an already generated option (i.e., congruent in terms of associated behavior), or clearly not feasible in the situation. The inter-rater agreement on this categorization (between first and second author) was found to be very good (Cohen’s  $\kappa = .83$ ,  $p < .001$ ). For further analyses on the number of goal-directed and non-goal-directed responses, we used the mean of the two raters.

### Statistical Analyses

Potential differences between patients and control participants in demographic and cognitive measures as well as task performance were assessed using two-sample *t*-tests or Mann-Whitney-U tests for continuous and chi-square tests for categorical variables. Degrees of freedom were adjusted if inequality of variance had to be assumed according to Levene’s tests. Effect sizes of group differences are reported as Cohen’s *d* or *r*.

To investigate the sole effect of the experimental manipulation on the quantity of options generated and to explore potential differences between healthy controls and patients, we conducted a 2 (subjective stopping rule vs. maximum)  $\times$  2 (problem-solving vs. open scenario)  $\times$  2 (HC vs. patient group) repeated measures analysis of variance (ANOVA). Post hoc pairwise comparisons were conducted to explore specific differences. Effect sizes of the ANOVAs are reported as partial Eta-squared ( $\eta^2$ ).

To explore associations of option generation with clinical variables, we computed Pearson correlation coefficients (*r*). Although conditions for using parametric statistics were met, the relatively small sample size leads us to additionally report Spearman correlations (*r<sub>s</sub>*) for the main analyses. We then performed Steiger tests for dependent correlation coefficients to test for potential differences in these correlations (Meng, Rosenthal, & Rubin, 1992; Steiger, 1980). To further analyze the specificity of the effect of apathy on option generation in relation to other

symptom dimensions, we computed a multiple linear regression model with symptoms that were significantly correlated with option generation as independent variables and option generation as dependent variable. We further asked whether the linkage between apathy and option generation could be mediated by cognitive deficits using hierarchical regression analysis (Baron & Kenny, 1986). According to the Baron and Kenny approach, a variable is considered to be a mediator (M) if (1) the independent variable (IV) significantly predicts the dependent variable (DV); (2) the IV significantly predicts M; and in a regression model with both IV and M predicting the DV (3) M significantly predicts the DV and (4) the IV predicts the DV less strongly than in (1). If conditions for potential mediation were met, we tested the statistical significance of the indirect (i.e., mediating) effect using bootstrapping procedures (Hayes, 2013). Moreover, we computed an additional Steiger Test and a multiple regression model with mean number of goal-directed options and verbal fluency as IV and apathy as DV to explore which task measure was more strongly associated with apathy.

Statistical tests report two-sided  $p$ -values and were computed with SPSS version 22 (IBM Corp., Armonk, NY).

## Results

### Sample Characteristics

Demographic, clinical, cognitive, and option generation measures, and group comparisons thereof are reported in Table 1. Both groups generated fare more goal-directed than non-goal-directed options. Patients generated significantly fewer total options,  $t(49) = 6.01$ ,  $p < .001$ ,  $d = 1.64$ , goal-directed,  $t(49) = 5.93$ ,  $p < .001$ ,  $d = 1.63$ , and non-goal-directed options,  $t(49) = 2.44$ ,  $p = .02$ ,  $d = .72$ , compared to healthy control participants. However, patients did not

significantly differ from control participants regarding the ratio of goal-directed versus non-goal-directed options,  $U = 288.50$ ,  $p = .61$ ,  $r = .07$ .

### Group analyses

To investigate overall effects of the experimental manipulation and at the same time compare the HC to the patient group, we conducted a  $2 \times 2 \times 2$  repeated measures ANOVA (Figure 1). There was a significant main effect of group,  $F(1, 49) = 35.21$ ,  $p < .001$ ,  $\eta^2 = .42$ , indicating that patients generated fewer options than healthy controls ( $M_{HC} = 5.58$ ,  $SD_{HC} = 1.50$ ;  $M_{patients} = 3.50$ ,  $SD_{patients} = 1.01$ ). Please note that the main effect of group remained significant when cognitive test scores (see Table 1) were included as covariates,  $F(1, 44) = 8.30$ ,  $p = .006$ ,  $\eta^2 = .16$ . The main effect of the factor “subjective stopping rule vs. maximum” was also significant,  $F(1, 49) = 105.73$ ,  $p < .001$ ,  $\eta^2 = .68$ , indicating that more options were generated in the maximum condition compared to when subjects terminated option generation on subjective grounds. We also found a significant main effect of the factor “problem-solving vs. open”,  $F(1, 49) = 81.22$ ,  $p < .001$ ,  $\eta^2 = .62$ , indicating that more options were generated in the open compared to problem-solving scenarios. There was further a significant two-way interaction between the two experimental factors “subjective stopping rule vs. maximum” and “problem-solving vs. open”,  $F(1, 49) = 66.64$ ,  $p < .001$ ,  $\eta^2 = .58$ . Moreover, we found an interaction between group and “subjective stopping rule vs. maximum”,  $F(1, 49) = 35.12$ ,  $p < .001$ ,  $\eta^2 = .42$ . This interaction effect reflects the fact that groups differentially increased the quantity of generated options due to encouragement in the maximum condition (HC > patients). We also found a two-way interaction between group and “problem-solving vs. open”,  $F(1, 49) = 11.06$ ,  $p = .002$ ,  $\eta^2 = .18$ , indicating that the HC group increased the quantity of generated options in open relative to problem-solving scenarios more strongly than patients. Finally, also the three-way

interaction was significant,  $F(2, 48) = 11.85, p = .001, \eta^2 = .20$ , reflecting the fact that group differences were most pronounced in the factor combination maximum/open. Follow-up pairwise comparisons revealed that the HC group generated more options than patients in all four factor combinations (all  $ps < .001$ ; see Figure 1).

The patient group ( $M = 35.67, SD = 9.85$ ) did not differ significantly from the HC group ( $M = 39.87, SD = 29.15$ ) regarding mean time taken to generate options averaged over all scenarios,  $t(23.22) = -.64, p = .53, d = -.19$ , but generated significantly less options per second,  $t(20.01) = 2.86, p = .01, d = 1.28$ .

### **Psychopathology and Option Generation**

Correlation coefficients between option generation indices and symptom ratings are listed in Table 2. None of the symptom variables were significantly associated with the mean amount of non-goal-directed options generated. The following analyses regarding psychopathology thus refer to goal-directed options. We observed a strong negative correlation between apathy, as assessed by the BNSS, and mean number of generated goal-directed options,  $r(28) = -.65, p < .001, r_s(28) = -.67, p < .001$  (see Figure 2A). In other words, apathy was associated with a reduced quantity of generated options. This association was also found when apathy was rated by a member of the nursing team based on the daily observation of the patient (AES),  $r(27) = -.53, p = .003, r_s(27) = -.64, p < .001$ . The diminished expression factor of the BNSS was also significantly correlated with mean number of generated goal-directed options,  $r(28) = -.40, p = .03, r_s(28) = -.42, p = .02$  (see supplementary Table S1 for correlations of option generation quantity with individual symptom subscales of the BNSS). However, apathy was more strongly associated with mean number of generated goal-directed options than diminished expression on a trend-level according to a Steiger-Test,  $z = 1.77, p = 0.08$ . Please note that

positive symptoms, depressive symptoms, and chlorpromazine equivalents (CPZ) were not significantly associated with any option generation indices and are thus not included in further analyses (all  $ps > .14$ ). The results of a multiple regression of the two negative symptom factors apathy and diminished expression on option generation,  $R^2 = .42$ ,  $F(2,29) = 9.72$ ,  $p = .001$ , indicated that apathy significantly predicted option generation,  $\beta = -.63$ ,  $t(29) = -3.47$ ,  $p = 0.002$ , whereas diminished expression did not reach significant predictive power,  $\beta = -.03$ ,  $t(29) = -0.17$ ,  $p = 0.87$ . In sum, our results suggest that the symptom apathy is the symptom dimension most strongly associated with the amount of generated goal-directed options.

### **Cognition and Option Generation**

We computed Pearson correlation coefficients between cognitive variables and option generation (see Table 2). The following test scores were significantly correlated with mean number of goal-directed options generated: verbal fluency (phonemic & semantic combined),  $r(28) = .50$ ,  $p = .005$ ,  $r_s(28) = .47$ ,  $p = .009$ , verbal crystallized intelligence (MWT-B),  $r(28) = .45$ ,  $p = .01$ ,  $r_s(28) = .38$ ,  $p = .04$ , and ideation fluency (Brick item of the Alternate Uses Test),  $r(28) = .40$ ,  $p = .03$ ,  $r_s(28) = .49$ ,  $p = .006$ . Interestingly, mean number of non-goal-directed options was only significantly correlated with the cognitive measure of ideation fluency,  $r(28) = -.65$ ,  $p < .001$ ,  $r_s(28) = -.45$ ,  $p = .01$ .

To test for possible mediation effects of assessed cognitive variables between apathy and option generation, we used hierarchical regression analysis. The only cognitive variable that fulfilled the criteria of potential mediation according to Baron and Kenny (1986), was verbal fluency (see *Statistical Analyses* for criteria). In particular, verbal fluency was the only cognitive variable that significantly correlated with apathy symptoms,  $r(28) = -.43$ ,  $p = .02$ . Neither verbal crystallized intelligence,  $r(28) = -.14$ ,  $p = .48$ , nor ideation fluency,  $r(28) = -.20$ ,  $p = .30$ , was

significantly correlated with apathy. Thus only verbal fluency was formally tested for mediation (see Figure 2B). Importantly, the relationship between apathy and mean quantity of goal-directed options remained significant ( $p < .01$ ) even when verbal fluency was used as a predictor in the multiple regression analysis, indicating that the relationship between apathy and mean quantity of goal-directed options generated was only partially mediated by verbal fluency. As Figure 2B illustrates, the standardized indirect effect was  $(-.43)(.50) = -.22$ . We tested the significance of this indirect effect using bootstrapping procedures (Hayes, 2013). Unstandardized indirect effects were computed for each of 10,000 bootstrapped samples, and the 95% confidence interval was computed by determining the indirect effects at the 2.5<sup>th</sup> and 97.5<sup>th</sup> percentiles. The bootstrapped unstandardized indirect effect was  $-.02$  and the 95% confidence interval ranged from  $-.05$  to  $.002$ . Thus, the indirect effect was statistically significant. However, the standardized direct effect of apathy on option generation remained highly significant, which indicates that the relationship between apathy and option generation was only partially mediated by verbal fluency. In other words, in addition to the strong direct relationship between apathy and mean quantity of goal-directed options (i.e., direct effect,  $\beta = -.53$ ,  $p = .002$ ), there was also a weaker but significant mediating effect of verbal fluency ( $\beta = -.22$ ).

The mean quantity of goal-directed options,  $r(28) = -.65$ ,  $p < .001$ , and verbal fluency,  $r(28) = -.43$ ,  $p = .02$ , were significantly associated with apathy symptoms. The other cognitive variables were not significantly associated with apathy, all  $ps > .30$  (see Table 2), and significantly smaller than the correlation of mean quantity of goal-directed options, all  $ps < .02$ . A Steiger Test revealed no significant difference between these correlations of apathy with mean quantity of goal-directed options and verbal fluency,  $Z = 1.47$ ,  $p = .14$ . However, a multiple regression of verbal fluency and mean quantity of goal-directed options on apathy,  $R^2 = .43$ ,  $F(2,$



29) = 10.40,  $p < .001$ , indicated that mean quantity of goal-directed options significantly predicted apathy,  $\beta = -.58$ ,  $t(29) = -.34$ ,  $p = .002$ , whereas verbal fluency did not significantly predict apathy,  $\beta = -.15$ ,  $t(29) = -.87$ ,  $p = .39$ . In sum, although the correlations of mean quantity of goal-directed options and verbal fluency with apathy are not significantly different, the multiple regression analysis suggests that mean quantity of goal-directed options is more strongly linked to apathy than verbal fluency.

### **Effects of Within-Subject Experimental Manipulation**

Correlation coefficients of apathy with mean number of generated goal-directed options in the four within-subject conditions were all highly significant, all  $ps < .001$ . Pairwise comparisons of the correlations in each of the two factors were non-significant according to Steiger tests for dependent correlation coefficients, “subjective stopping rule vs. maximum”:  $z = -.73$ ,  $p = .47$ , “problem solving vs. open scenarios”:  $z = 1.24$ ,  $p = .22$ . In other words, there were no significant differences in the correlations between apathy and quantity of goal-directed options generated due to our  $2 \times 2$  within-subject experimental manipulation.

### **Option Generation Time**

Further correlational analyses revealed no significant association of apathy with how long participants generated options on average,  $r(28) = -.21$ ,  $p = .26$ . However, patients with more pronounced apathy symptoms generated less options per time unit (i.e., lower frequency of options),  $r(28) = -.45$ ,  $p = .01$ .

## **Discussion**

Negative symptoms in schizophrenia can be split up into the two factors of apathy and diminished expression. Particularly apathy seems to be linked to poor functional outcome. Recently, apathy in schizophrenia has been approached as a disorder of decision-making (e.g.,

Fervaha, Graff-Guerrero, et al., 2013; Hartmann et al., in press; Heerey et al., 2008). In the present study, we hypothesized that apathy is associated with predecisional deficits, that is, deficits in the generation of options for action in ill-structured real world scenarios. We have three key findings to report. First, patients generated significantly fewer goal-directed options than healthy control participants. Second, we found a strong negative correlation of apathy symptom severity in patients with the quantity of generated goal-directed options. Among all measures of psychopathology assessed in the current study (including diminished expression), option generation was most strongly linked to apathy symptoms. Third, this link was only partially mediated by apathy-dependent deficits in verbal fluency. Thus, these data suggest a potentially important role of option generation as a specific predecisional mechanism contributing to apathetic states in schizophrenia.

In the current study, we experimentally manipulated two factors – the stopping rule (subjective stopping rule vs. maximum) and the type of scenario (problem-solving vs. open). Pairwise comparisons showed that neither the stopping rule, nor the type of scenario did significantly affect the correlation of apathy with quantity. However, all correlation coefficients were strongly negative, emphasizing that apathy is linked to deficient generation of options in various contexts. Thus, our secondary hypotheses – a stronger association of apathy with quantity of generated goal-directed options under the subjective compared to the maximum stopping rule applied and in open compared to problem-solving scenarios – could not be confirmed in this study.

Group differences regarding amount of goal-directed options were significant in all conditions (patients < HC), however they were more pronounced in the maximum stopping rule condition compared to when subjects were free to stop and more pronounced in open relative to

problem-solving scenarios. In other words, our experimental manipulation of stopping-rule and type of scenario impacted option generation more strongly in healthy controls compared to patients. The differential effect of the stopping-rule might either be explained by a genuinely smaller repertoire of options for action in patients or a failure to motivate further option generation due to a social prompt (maximum condition). The differential effect of type of scenario on the other hand is consistent with clinical observations that schizophrenia patients seem to be most strongly affected in open situations where behavior has to be initiated to satisfy personal goals and motives (Treméau et al., 2012). One could speculate that this reflects an inability to generate more options as the hypothetical option space widens (problem-solving vs. open). In sum, patients did not adjust the amount of options generated as strongly as healthy controls in response to experimental manipulations.

It has been proposed that apathy in neuropsychiatric patients can be divided into three subtypes of disrupted processing: motivational (linking emotional-affective signals with behavior), cognitive, and auto-activation (Levy & Dubois, 2006). While auto-activation deficits are primarily observed in patients with basal ganglia lesions, compelling evidence points to motivational deficits in schizophrenia patients with apathy (for a recent review see Strauss, Waltz, & Gold, 2014). Option generation is a cognitive process occurring in a predecisional stage. The role of cognitive dysfunction in the pathogenesis of apathy in schizophrenia remains a matter of debate. Cognitive domains commonly associated with apathy are processing speed, verbal fluency, verbal memory, and working memory (e.g., Berman et al., 1997; Bozikas, Kosmidis, Kioperlidou, & Karavatos, 2004; O'Leary et al., 2000). However, the association seems to be moderate at the most, requiring meta-analytic approaches to achieve the required power (Dibben, Rice, Laws, & McKenna, 2009; Heinrichs & Zakzanis, 1998; Keefe et al., 2006).

One possible explanation for this pattern might be that prior research has not specifically investigated cognitive processes that are directly linked to everyday decision-making and goal-directed behavior (Levy & Dubois, 2006). In contrast to the moderate associations of apathy with cognition in previous studies, we found a strong correlation of apathy with quantity of generated options in our task involving ill-structured everyday scenarios. Moreover, it has to be considered that, in contrast to some cognitive tests our option generation task was implemented in the same modality as the clinical interview (verbal). Additionally, our task was run with a very generous time limit, which is rarely the case in cognitive test batteries. This allowed assessing deficits beyond reduced processing speed. In sum, the strong link between apathy and option generation suggests that deficits in option generation might partially cause or perpetuate apathy symptoms.

In addition to framing deficient option generation as a predecisional cognitive deficit, one could also view the present findings as a motivational deficit as mentioned above. In particular, they are in line with previously reported dysfunctional cost-benefit decision-making in schizophrenia (Fervaha, Graff-Guerrero, et al., 2013; Gold et al., 2013; Hartmann et al., in press). When generating options for action, the agent has to dynamically weigh the potential increase in future reward that might come with additional options against the cost of time and cognitive effort that have to be invested in the generation process. Thus, one should stop to generate options when expected costs outweigh expected benefits (Gigerenzer & Todd, 1999). There is evidence for degraded reward value representations (Gold, Waltz, Prentice, Morris, & Heerey, 2008) and overweighing of time (Heerey, Robinson, McMahon, & Gold, 2007) and effort costs (Gorissen, Sanz, & Schmand, 2005; Hartmann et al., in press) in decisions of patients with schizophrenia. It is therefore possible to approach the quantitative reduction in option generation

from the viewpoint of dysfunctional cost-benefit decision-making, that is, the effort of generating new options is overweighted in relation to their potential benefits.

In the course of data processing in the current study, we categorized the participants' responses into goal-directed and non-goal-directed options. None of the assessed symptoms were associated with the generated amount of non-goal-directed options. Interestingly, the only cognitive measure that was significantly correlated with amount of non-goal-directed options was ideation fluency. This is a potential hint towards how "option generation fluency" differs from ideation fluency. In option generation, the agent primarily aims to gather a sufficient amount of feasible options for concrete goal-directed action; while in creative ideation fluency feasibility plays a negligible role. It is likely that fluency in option generation and ideation depends on partially overlapping processes, the current study, however, also provides evidence for the notion that option generation and ideation are conceptually different processes.

In the current study, we assumed that if an agent generates more options, the decision outcome would be better and should lead to an increase in goal-directed behavior. This is in line with the classical notion that a complete "option space" or "option tree" is beneficial for optimal decision-making in complex situations (Adelman, 1987; Gettys et al., 1987; Keller & Ho, 1988). More recently, some authors (Klein et al., 1995; Raab & Johnson, 2007) have suggested that in constrained situations highly trained experts (e.g., athletes and chess players) need not extensively generate and evaluate options for a satisfactory outcome because their first ones are usually the best ("take-the first-heuristic", "less-is-more"). However, our premise is in general agreement with recent studies on option generation in non-clinical populations, which have applied less structured scenarios (Ward, Suss, Eccles, Williams, & Harris, 2011; Ward, Torof, Whyte, Eccles, & Harris, 2010). It is thus conceivable that highly automated expert decisions

differ qualitatively from decision situations people face in everyday ill-structured environments, the latter requiring more options to arrive at optimal decisions.

In our study, we used scenarios with very few constraints in order to emulate real-world situations. In these situations apathetic patients show a decreased quantity of generated options. However, a consequence of using real-world scenarios is that assessment of option quality is rendered highly problematic. Because our scenarios did not contain an optimal or near optimal solution, quality assessment was not possible. An alternative to task-based assessment is the interview-based assessment of real-world problem-solving skills, which have been shown to be negatively associated with negative symptoms in schizophrenia (Revheim et al., 2006).

Some limitations of the current study should be addressed. First, sample size was rather modest and thus our results need to be replicated in a larger sample. Second, we used relatively strict exclusion criteria in order to reduce possible confounding factors. Therefore, replication should also address the question of generalizability to a broader population of patients with schizophrenia. Third, our study design is correlational and therefore does not allow to make causal statements. One explanation of our data could be that disease specific pathophysiological mechanisms lead to deficits in option generation, which then cause a reduction in goal-directed behavior (i.e., apathy). However, one could also speculate that deficits in option generation reflect the fact that apathetic individuals have experienced less variance in behavior in specific decision situations (due to an underlying disease mechanism) and thus cannot retrieve as many options for action from long-term memory. Importantly, regardless of not yet clarified causality the current study adds to the growing knowledge of apathetic phenomena.

From a more practical perspective, we believe that our findings have potential clinical implications. For example, the training of option generation could be implemented in a combined

cognitive remediation (Wykes, Huddy, Cellard, McGurk, & Czobor, 2011) and psychotherapy setting (Drake et al., 2013). Patients could, for instance, be trained in a computerized option generation task while transfer to everyday life would be targeted in therapy sessions. Future studies could test the applicability and efficacy of such option generation trainings in clinical settings. Independent of this, the current study provides empirical support for the potential importance of predecisional stages in decision-making for the development of neuropsychiatric symptoms, particularly apathy.

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Table 1

*Demographic and clinical characteristics and cognitive test scores*

	Healthy controls (n = 21)	Patient group (n = 30)	p-value (t/ $\chi^2$ )
<i>Demographics</i>			
Age (years)	32.33 (6.70)	30.33 (8.47)	.37
Gender (male/female)	16/5	23/7	.97
Handedness (r/l)	17/4	28/2	.18
Education (years) <sup>a</sup>	12.55 (3.98)	9.98 (1.65)	< .01
<i>Clinical variables</i>			
CPZ equivalents <sup>b</sup>	-	563.83 (419.56)	-
Duration of illness (years)	-	9.74 (8.06)	-
Apathy (BNSS) <sup>c</sup>	-	15.77 (6.16)	-
Diminished expression (BNSS) <sup>c</sup>	-	10.23 (6.46)	-
PANSS positive <sup>d</sup>	-	7.00 (2.80)	-
PANSS negative <sup>d</sup>	-	13.83 (4.76)	-
PSP scale	-	54.07 (10.13)	-
CDSS	-	2.27 (2.29)	-
<i>Cognitive test scores<sup>e</sup></i>			
Verbal memory retrieval	0 (1)	.15 (1.50)	.69
Processing speed	0 (1)	-1.29 (.89)	< .001
Verbal fluency composite (phonemic & category fluency)	0 (1)	-1.15 (.76)	< .001
Crystallized verbal intelligence	0 (1)	-1.19 (1.69)	< .01
Ideation fluency	0 (1)	-.44 (.69)	.07
<i>Option generation indices</i>			
Goal-directed options <sup>f</sup>	5.58 (1.50)	3.50 (1.01)	< .001
Non-goal-directed options <sup>f</sup>	.28 (.18)	.17 (.15)	< .05
Total options <sup>f</sup>	5.86 (1.57)	3.67 (1.04)	< .001
Ratio non-goal-directed/goal-directed <sup>f</sup>	.05 (.03)	.05 (.04)	.61 <sup>g</sup>

*Note.* Data are presented as means and standard deviations. CPZ = Chlorpromazine; BNSS = Brief Negative Symptom Scale; PANSS = Positive and Negative Syndrome Scale; PSP = Personal and Social Performance; CDSS = Calgary Depression Scale for Schizophrenia. <sup>a</sup>Compulsory education in Switzerland is 9 years. <sup>b</sup>All patients were receiving atypical antipsychotics at the time of testing. Two individuals were additionally medicated with low doses of typical antipsychotics. 6 were receiving an SSRI, 3 were receiving low doses of benzodiazepine, 1 was receiving a mood stabilizer, 2 were receiving zolpidem against insomnia. <sup>c</sup>Apathy: average of anhedonia, asociality, avolition; diminished expression: average of blunted affect, alogia. <sup>d</sup>Positive factor: P1, P3, P5, G9; negative factor: N1, N2, N3, N4, N6, G7. <sup>e</sup>Cognition data has been z-transformed based on the data of the HC group for each test separately. <sup>f</sup>Across all scenarios. <sup>g</sup>Mann-Whitney-U test was computed because of non-normality of the variable ratio non-goal-directed/goal-directed options.

Table 2

*Pearson correlations between option generation indices, clinical variables, and cognitive test scores*

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. Goal-Directed Options	1																
2. Non-Goal-Directed Options	.14	1															
3. Total Options	.99***	.28	1														
4. Ratio Non-Goal-Directed/Goal-Directed	-.13	.95***	.01	1													
5. Apathy (BNSS)	-.65***	.23	-.59***	.20 <sup>a</sup>	1												
6. Diminished Expression (BNSS)	-.40*	.24	-.35	.14 <sup>a</sup>	.59**	1											
7. Apathy (AES)	-.53**	.19	-.48**	.25 <sup>a</sup>	.64***	.50**	1										
8. PANSS Negative Symptoms	-.48**	.35	-.41*	.23 <sup>a</sup>	.70***	.88***	.65***	1									
9. PANSS Positive Symptoms	-.10	.23	-.06	.31 <sup>a</sup>	.19	.08	.23	.25	1								
10. Depressive Symptoms (CDSS)	-.17	.18	-.14	.21 <sup>a</sup>	.18	-.02	.21	.17	.20	1							
11. Personal and Social Performance (PSP)	.52**	-.34	.45*	.25 <sup>a</sup>	-.80***	-.62**	-.66***	-.67***	-.30	-.01	1						
12. CPZ Equivalents	-.28	-.14	-.29	.05 <sup>a</sup>	.06	-.04	.13	.01	.43*	.02	-.06	1					
13. Verbal Memory Retrieval	-.19	.03	-.18	-.03 <sup>a</sup>	.16	.13	.44*	.17	.20	.01	-.23	.23	1				
14. Processing Speed	.18	.01	.18	.01 <sup>a</sup>	-.17	-.36	-.29	-.25	-.15	.16	-.22	-.26	-.14	1			
15. Verbal Fluency Composite (phonemic & category fluency)	.50**	.01	.48**	-.19 <sup>a</sup>	-.43*	-.64***	-.36	-.52**	.08	.01	.42*	-.04	-.18	.28	1		
16. Crystallized Verbal Intelligence	.45*	.14	.46*	-.03 <sup>a</sup>	-.14	-.23	-.32	-.26	-.07	-.39*	.01	.10	-.10	.18	.36	1	
17. Ideation Fluency	.40*	.46*	.46*	.27 <sup>a</sup>	-.20	-.47**	-.30	-.38*	.15	.07	.18	-.10	.10	.29	.43*	.42*	1

Note.  $N = 30$ . BNSS = Brief Negative Symptoms Scale; AES = Apathy Evaluation Scale; PANSS = Positive and Negative Syndrome Scale; CDSS = Calgary Depression Scale for Schizophrenia; CPZ = Chlorpromazine. <sup>a</sup> Spearman instead of Pearson correlation was computed because of non-normality of variable 4. \* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$ .

### Figure Captions

*Figure 1.* Mean quantity of generated options in the four within-subjects conditions (subjective stopping rule vs. maximum × problem-solving vs. open scenario) in the healthy control group (HC) and the patient group. Error bars represent standard error of the mean. \*\*\*  $p < .001$ .

*Figure 2. A.* Scatterplot and correlation coefficient between apathy and mean quantity of generated goal-directed options across all 20 scenarios. *B.* Standardized regression coefficients for the relationship between apathy and mean quantity of goal-directed options generated as mediated by verbal fluency. The standardized regression coefficient between apathy and option generation, holding verbal fluency constant, is in parentheses. BNSS = Brief Negative Symptom Scale. \*  $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$ .



